



Panic Panic

Consensus Statement

NIH Consensus Development Conference
September 25–27, 1991

Volume 9 Number 2

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Introduction

Panic disorder with and without agoraphobia is a debilitating condition that will afflict at least 1 out of every 75 people in this country and worldwide during their lifetime. Panic attacks are characterized by sudden and unexpected discrete periods of intense fear or discomfort associated with shortness of breath, dizziness, palpitations, nausea, or abdominal distress. During an attack people often believe that they are having a heart attack or, alternately, that they are losing their mind. Panic sufferers often develop agoraphobia secondary to the occurrence of these unexpected panic attacks. Consequently, they begin to avoid places where they fear a panic attack may occur or where help would be difficult to obtain. If the agoraphobia becomes severe enough, a person may become housebound.

A growing body of knowledge indicates that some medications and selected psychosocial treatments are effective for panic disorder, with and without agoraphobic avoidance. Two classes of antidepressants (i.e., tricyclics and monamine oxidase inhibitors) as well as certain high-potency benzodiazepines (e.g., alprazolam, lorazepam, and clonazepam) have been found to be effective in reducing or eliminating panic attacks associated with the various forms of panic disorder. Substantial research efforts continue the search for other medications useful in the treatment of these conditions. Initial indications are that some of these other agents, particularly the serotonin uptake blockers, may be effective panic medications. The pharmacological agents may present problems such as undesirable side effects, the risk of dependence, and a significant relapse rate once medication is discontinued.

Several variations and combinations of behavioral and cognitive treatment approaches also have demonstrated efficacy in the reduction and/or elimination of panic attacks and agoraphobia. Early reports of research specifically targeting panic attacks indicate that significant numbers of patients are panic-free at the end of cognitive-behavioral treatment and remain so at a 2-year followup.

Information is sparse on such issues as (1) the effectiveness of combined psychosocial and pharmacological treatments, (2) the mechanisms of therapeutic action, (3) demographic and

other patient factors that may predict responsiveness to either class of treatment, (4) the long-term effectiveness of treatments for panic disorder once treatment stops, and (5) the value of these treatments for those patients who suffer from panic disorder in combination with other psychological and psychiatric disorders. The latter group represents a significant segment of those people suffering from panic disorder.

To help resolve questions surrounding these and other issues, the Office of Medical Applications of Research of the National Institutes of Health in conjunction with the National Institute of Mental Health convened a Consensus Development Conference on the Treatment of Panic Disorder on September 25-27, 1991. Following a day and a half of presentations by experts in the relevant fields and discussion from the audience, a consensus panel comprising experts in psychology, psychiatry, cardiology, internal medicine, and methodology, as well as members of the general public, considered the scientific evidence and formulated a consensus statement that addressed the following five questions:

- What are the epidemiology, natural history, and course of panic disorder with and without agoraphobia? How is it diagnosed?
- What are the current treatments? What are the short-term and long-term effects of acute and extended treatment of this disorder?
- What are the short-term and long-term adverse effects of these treatments? How should they be managed?
- What are considerations for treatment planning?
- What are the significant questions for future research?

What Are the Epidemiology, Natural History, And Course of Panic Disorder With and Without Agoraphobia? How Is It Diagnosed?

What Is Panic Disorder?

Beginning in the 1960's, investigators and clinicians began to differentiate patients who had unexpected anxiety attacks from patients with other anxiety disorders. The diagnostic category of panic disorder was first officially recognized with the publication of *Diagnostic and Statistical Manual of Mental Disorders* (3rd edition) of the American Psychiatric Association in 1980 (DSM-III). These criteria were modified slightly with the 1987 publication of the revised version of the *Diagnostic Manual*, DSM-III-R.

Fundamental to the diagnosis of panic disorder is the occurrence of panic attacks. These attacks consist of discrete periods of intense fear or discomfort in which at least four of the symptoms noted below develop abruptly and reach a crescendo within 10 minutes, typically lasting 10 minutes or so. Attacks may recur repeatedly and rapidly, however, once these symptoms abate, severe anxiety may last for many hours. The symptoms include:

- shortness of breath (or smothering sensations)
- dizziness, unsteady feelings, or faintness
- palpitations or accelerated heart rate (tachycardia)
- trembling or shaking
- sweating
- choking
- nausea or abdominal distress
- depersonalization or derealization
- numbness or tingling sensations (paresthesias)
- flushes (hot flashes) or chills
- chest pain or discomfort
- fear of dying
- fear of going crazy or doing something uncontrolled

Panic attacks may occur as rare isolated incidents that cause little or no sustained impact on the individual's functioning or

as clusters of attacks with adverse effects. They also occur during sleep.

To satisfy the diagnostic criteria for panic disorder, at least some of the panic attacks must occur unexpectedly or spontaneously, that is, in the absence of specific environmental or situational triggers such as elevators, public speaking, snakes, closed spaces, or other situations that evoke fearful avoidance in some people. Further, the diagnostic criteria require either a clustering of at least four attacks spread over a 4-week period or one or more attacks followed by at least 1 month of fearful anticipation of experiencing more such attacks.

Although research is under way to test and refine these criteria, there is a broad consensus that panic disorder, as currently defined, is a distinct condition with a specific presentation, course, positive family history, complications, and response to treatment.

Panic disorder must be differentiated from other disorders that may share similar clinical features. At this time, diagnosis is dependent on a detailed clinical assessment of the presenting complaints and history because there are no specific laboratory tests. A medical workup is recommended to rule out other conditions. At the same time, the risk of misdiagnosis leading to costly medical investigations and delays in treatment for panic disorder must also be guarded against.

Currently, two main subtypes of panic disorder are widely recognized and codified in DSM-III-R. These subtypes vary in the severity and extensiveness of phobic avoidance: panic disorder without agoraphobia and panic disorder with agoraphobia. In cases of panic disorder with agoraphobia, there is avoidance of places or situations from which escape might be difficult or embarrassing or in which help might not be available in the event of a panic attack. The degree of avoidance may vary from mild to moderate or, at the extreme, to a constricted lifestyle imposed by severe avoidance, resulting in the individual's being nearly or completely housebound or otherwise severely dysfunctional.

Investigators are seeking to develop additional ways of subtyping panic disorder based on the phenomenology, age of onset, response to treatment, etc., which may have implications for etiology, diagnosis, and treatment.

Differential Diagnosis: Separating Panic Disorders From Other Disorders

There are many other disorders in which panic attacks may occur. The more common are simple phobia (in which the panic occurs immediately before or upon exposure to the feared situation and nowhere else) and social phobias in which they occur only when individuals feel they are the focus of others' attention (e.g. while eating). Other disorders that should be considered in differential diagnosis include claustrophobia; severe depression; dissociative disorders; generalized anxiety without panic; alcohol or drug withdrawal; stimulant abuse (caffeine, cocaine, amphetamines); physical disorders such as cardiac, adrenal, vestibular, thyroid, or seizure disorders.

Epidemiology and Course

Panic disorder is relatively common; similar rates have been found in many countries in international studies. Approximately one third of the individuals with panic disorder also have agoraphobia, although in clinical settings, the majority present with some agoraphobia. Panic disorder with agoraphobia is diagnosed about twice as frequently in females as in males.

The most common age of onset is middle teens and early adulthood; however, panic disorder may onset at any time. A common pattern of onset is the occurrence of occasional unexpected panic attacks that then increase in frequency and are associated with mounting fears of having subsequent attacks. Over time there is often a pattern of spreading fearful avoidance.

Little is known about the long-term course of this disorder. The limited findings to date suggest that in most cases it is a chronic disorder that waxes and wanes in severity. However, some people may have a limited period of dysfunction that never recurs, while others may experience a severe chronic form of the disorder. Those with agoraphobia tend to have a more severe and complicated course. Treatment early in the development of this disorder may shorten the duration and may prevent complications, including agoraphobia and depression.

Comorbidity: Associated Disorders

Certain conditions have been found to be associated with panic disorder, particularly in those individuals with long-standing panic attacks and agoraphobia. These conditions include abuse of alcohol and drugs, depression, and other anxiety and personality disorders. Other medical disorders that occur more commonly in patients with panic disorder may include atypical chest pain, irritable bowel syndrome, asthma, and migraine.

What Are the Current Treatments? What Are The Short-Term and Long-Term Effects of Acute and Extended Treatment of This Disorder?

Panic disorder is a treatable condition. The effectiveness of treatment should be evaluated on a number of dimensions: (1) acceptance and tolerance by patients; (2) reduction or elimination of panic attacks, reduction of clinically significant anxiety and disability secondary to phobic avoidance, amelioration of other common comorbid conditions such as depression; and (3) long-term prevention of relapse.

Several different classes of treatment have been shown to be clinically effective, including cognitive and behavioral, pharmacologic, and combinations of the two. The most commonly used behavioral approach is graduated exposure, aimed primarily at reducing phobic avoidance and anticipatory anxiety. Cognitive behavioral approaches, developed more recently, also treat panic attacks directly. These treatments involve cognitive restructuring, that is, changing of maladaptive thought processes and are generally used in combination with a variety of behavioral techniques, including breathing retraining and activities that target exposure to bodily sensations and external phobic situations. Ongoing assignments to practice the techniques are made by the therapist. These treatments seem to be well accepted by patients and typically involve weekly sessions for 8 to 12 weeks. Initial improvement is noted in many patients within 3 to 6 weeks of beginning treatment. Among the various psychotherapeutic approaches, combined treatments that include cognitive therapy in addition to other techniques appear to be most effective, especially in reducing panic attacks. Longer term followup of these interventions suggests a low relapse rate.

Pharmacologic treatments include tricyclic antidepressants, monoamine oxidase (MAO) inhibitors, and high-potency benzodiazepines. A significant proportion of patients do not easily tolerate certain of the tricyclics, whereas benzodiazepines are better accepted. Patients who tolerate tricyclics show significant improvement, with a reduced number of panic attacks during the period of treatment, ranging from 8 to 32 weeks in controlled trials. Benzodiazepines have a rapid onset

of action with immediate reduction of panic symptoms, whereas antidepressants require 3 to 6 weeks to achieve therapeutic effect. In addition, the action of benzodiazepines in reducing anxiety between attacks is thought advantageous by some clinicians. Careful titration of medication to effective therapeutic doses with gradual increase in dosage is necessary. Very gradual increases may be particularly important with tricyclics in order to reduce attrition. Longer term duration of treatment probably increases clinical response. Gradual tapering of all medications when treatment ends is strongly indicated. The relapse rate following termination of medication for antidepressants is moderate but is probably higher for benzodiazepines. The relatively high response rate to the control conditions (placebo) needs further examination.

Few studies have examined combined behavioral and pharmacologic methods. There is some evidence that a combination of tricyclics and exposure therapy may have additive effects in the short term, but there is no evidence for long-term advantage over either method alone. Currently, there are few published studies available that assess the combined effect of cognitive and pharmacologic intervention, nor has the optimal sequence of combined methods been examined satisfactorily. Whether using a combination of two effective methods improves upon the effectiveness of either alone or is less effective than either alone is not a settled issue.

There are no controlled data on efficacy of treatment for panic disorder or other widely used approaches, such as psychodynamic psychotherapy.

What Are the Short-Term and Long-Term Adverse Effects of These Treatments? How Should They Be Managed?

Adverse effects can be classified in a number of categories, including drug-related disturbances and other physical effects, adverse psychological and behavioral side effects, rebound effects (i.e., worsening of the disorder when treatment is removed), and misplaced confidence in unproven treatments that may preclude other treatments with a better chance of effectiveness. ...

The adverse effects discussed in this section are based on clinical research studies of panic disorder. It is unclear how and on what dimensions research patients may differ from the general clinical population; thus, the research samples may not be representative of the group of patients that present for treatment in a nonresearch, clinical setting.

In programs offering pharmacotherapy, individuals are not admitted to studies if they have preexisting medical conditions (including pregnancy) that would contraindicate the use of the medications under study. In both pharmacotherapy and cognitive-behavioral studies, individuals are typically referred elsewhere if the individual meets criteria for substance abuse.

Cognitive and Behavioral Treatments

Cognitive and behavioral treatments are ordinarily well tolerated when applied by skilled therapists. Dropout rates in controlled studies range from 5 to 8 percent in the cognitive-behavioral therapies and between 12 and 16 percent in the relaxation and *in vivo* exposure-based treatments. Therapies that include cognitive techniques may also address accompanying depression. Although very few adverse effects of these treatments have been reported, there have been some instances of panic attacks induced by relaxation. This can be counteracted by a more gradual approach to relaxation and teaching the patient techniques for controlling the relaxation procedure. No other adverse effects have been reported.

Other Psychotherapies

In the absence of any empirical studies examining the effectiveness of treatments other than cognitive and behavioral

therapies, no conclusions can be drawn about adverse effects. However, given that recent research results have identified useful pharmacotherapy and psychotherapy approaches, one risk of maintaining individuals in nonvalidated treatments of panic disorder is that misplaced confidence in the therapy's potential effectiveness may preclude application of more effective treatment. This can be particularly problematic with psychotherapy treatments if the nature of the therapeutic relationship makes it difficult for the patient to seek additional or alternate treatment. Psychotherapies without demonstrated effectiveness in panic, such as psychodynamic psychotherapy, however, may be helpful for other difficulties that the patient presents. Thus, when progress in the reduction of panic disorder is not apparent within 6 to 8 weeks, ancillary pharmacotherapy or cognitive behavioral treatment or a brief break in psychotherapy for these treatments should be considered.

Pharmacological Treatments

With three effective classes of pharmacological agents now available in the treatment of panic disorder, risks and benefits of each need to be considered.

Tricyclic antidepressants offer the benefit of once-a-day dosing, a low risk of dependence, and no dietary restrictions. They also have a concomitant antidepressant effect that is frequently helpful. Adverse effects include anticholinergic side effects, low blood pressure, overstimulation, and weight gain. Taken together, these effects may cause up to 35 percent of patients to discontinue treatment before therapeutic benefits occur.

The benefits of MAO inhibitors include, as with the tricyclics, an antidepressant effect and a low risk of dependence. However, the anticholinergic effects may be lower than for the tricyclics. Sexual difficulties, particularly problems in orgasm, may occur as do hypotension and weight gain. One added complication, which may be difficult for some patients, is the need to follow a low tyramine diet.

One benefit of the benzodiazepines, because they have a rapid onset of action, is that they can be used to treat surges of anticipatory anxiety or panic. This "as needed" use of benzodiazepines should not replace the use of sufficient daily doses when that is indicated. Risks include sedation and

psychomotor impairment. Benzodiazepines will interact with alcohol if it is not restricted. Although some of these adverse side effects largely subside after 4 to 6 weeks of treatment, subjective cloudiness may remain. The most serious risk with this class of medication is that of physical dependence. Withdrawal symptoms or a recurrence of panic symptoms during drug tapering is a definite risk with long-term treatment.

The attrition rate in pharmacologic studies varies with the drug under investigation. It is approximately 25 percent for the tricyclics, slightly lower for the MAO inhibitors, and approximately 15 percent for the high-potency benzodiazepines. Many of these dropouts appear directly related to the drug side effects. With imipramine, starting with a low dose and building up slowly may significantly reduce the risk of premature treatment termination. Similarly, the potential excessive use of benzodiazepines require caution in their use in individuals who have a history or risk of drug dependence. Care must be exercised in prescribing the tricyclic and the MAO inhibitor medications for individuals with cardiovascular disease; if acute relief is needed in such patients, high-potency benzodiazepines are the treatments of choice.

What Are Considerations for Treatment Planning?

The practicing clinician does not usually see panic disorder in its pure form. Further, because there are a number of different treatment strategies with similar treatment efficacy in the acute phase, the central question becomes not “What is the treatment of choice?” but, “What factors need to be considered in choosing optimum treatment?” Decisions need to be made regarding choice of single modality, concurrent, or sequential interventions.

Primary care physicians or other clinicians who identify patients with panic disorder will need to address the issue of potential referral for treatments specific to panic disorder with or without agoraphobia.

The factors that need to be considered by any clinician include degree of urgency, comorbid conditions, history, and patient fit and compliance issues.

Each of these groups of factors will be examined independently both in terms of the assessment data required and their implications for strategic interventions.

Degree of Urgency

There are cases of emergency such as medical complications secondary to the phobic fears (e.g., fear of swallowing leading to dehydration and weight loss), imminent loss of job or relationship, inability to undergo necessary medical procedures, children's welfare at risk, or acute and rapid generalization of phobic behavior. In such cases, mobilization of family resources or high-potency benzodiazepines may be the starting point for treatment once the patient has received basic educational information. This may be accompanied by cognitive-behavioral treatment, alternative medications, and other followup care. The patient's own subjective sense of urgency may or may not indicate a need for urgent intervention. A panic attack in and of itself is not an emergency. Common obsessive fears of losing control need to be carefully distinguished from actual imminent loss of control.

History

The history of the patient and his or her family will yield critical information for treatment planning. Is this the first episode or one in a lifetime series? Has the patient ever received the diagnosis before? What treatments have been tried in the past, and were they successful in some or any measure? Is there a family history of psychiatric disorder or substance abuse? Did the patient or the family engage in or respond to any treatment? Were there recent events that may have triggered the current onset of symptoms, such as surgery, illness, childbirth, miscarriage, trauma, loss, or external stressors? Are there any known developmental vulnerabilities such as a history of abuse or dysfunctional family? The need for and advisability of including family or significant others in the educational and/or treatment process should be assessed.

Comorbid Conditions

There are three kinds of medical conditions that may affect treatment planning and may need to be treated concurrently. These are (1) conditions that may affect the safety or efficacy of psychopharmacological treatments (such as some specific cardiovascular, pulmonary, gastrointestinal, or endocrine disorders; pregnancy; or lactation); (2) conditions with a prominent component of anxiety (such as thyroid disease, polycythemia, lupus, and pulmonary insufficiency); and (3)

conditions requiring treatment with medications such as vasoconstrictors, bronchodilators, or steroids, which may cause or exacerbate anxiety.

The necessity for a complete psychological assessment in addition to the medical workup cannot be overemphasized. Up to 70 percent of patients with panic disorder may have a comorbid psychological or psychiatric condition that will need to be included in the treatment planning and perhaps addressed therapeutically concomitantly or at a later point. A high percentage are depressed or demoralized secondary to suffering panic attacks but should be treated for panic first. Other conditions such as major depression, posttraumatic stress disorder, bipolar mood disorder, dissociative disorders, other anxiety disorders such as obsessive compulsive disorder or social phobia, eating disorders, or complex personality disorders may require concurrent treatment.

Finally, individuals need to be assessed explicitly regarding substance abuse, including alcohol, marijuana, opiates, hallucinogens, cocaine, over-the-counter drugs such as nasal sprays and diet pills, caffeinism, or benzodiazepine abuse. Patients in current withdrawal or active abuse must be treated for substance abuse before or concurrent with specific panic disorder treatment.

Patient Fit and Compliance Issues

The clinician, in consultation with the patient, should select one of the treatments with demonstrated efficacy or a combination as the initial treatment. Selection should be based on patient preference in the context of a comprehensive assessment of urgency, history, and comorbidity. It may be the case that the selected treatment will require referral, consultation, or supervision.

The individual with panic disorder needs to be an active, fully informed participant in the treatment planning process. Education and demystification is frequently needed. This means advising the patient not only of the short-term benefits and risks but also of long-term benefits and risks where known and addressing the issue of long-term relapse prevention. The patient's initial degree of relief and motivation following education may give direction to the next step. Attitudes and concerns regarding various treatment options must be explored

and negotiated. The patient's request in presenting for treatment must be kept in mind. Answering questions such as "why me?" or "why now?" or "what is this about?" may establish a better foundation for treatment.

Patients should be given education about the disorder and encouragement to re-enter phobic situations gradually when medication alone is chosen as the initial treatment. Current research suggests that an absence of any noticeable improvement after about 6 to 8 weeks of *any* treatment should suggest a reassessment, consultation, or change of modality.

Particularly for those patients for whom there has been a chronic course or a history of multiple episodes of acute symptomatology, recovery, and relapse, longer term strategies need to be considered following the acute phase of treatment. Unfortunately, at this time, little is known regarding the relative long-term efficacy of maintenance doses of medication, other psychotherapies, changes in lifestyle aimed at stress reduction, or participation in ongoing self-help groups. These current practices have been shown to be of value in other disorders and may in the future be shown to be so in panic disorder as well. As with many other treatable disorders, access to effective care is at times limited by regulatory decisions, lack of financial resources, inadequate third party coverage, and stigma.

What Are the Significant Questions for Future Research?

As would be expected in a relatively new field, many research questions remain, and each new finding is likely to stimulate further questions. Among the most important questions are the following:

Identifying Those at Risk

Although onset is known to be most frequent in adolescence and young adulthood, little is known about who is more likely to have an isolated attack, and, of those persons, who will go on to develop the full disorder, and what sequence of events may influence this. In this area, promising leads to follow are the investigation of temperament and personality; family and genetic patterns; developmental growth characteristics; and other biological, psychological, and environmental factors. Thus, both high-risk studies (e.g., children of high-risk families) and population studies are needed to answer these questions.

Course of Disorder

Much of the information currently available is derived from cross-sectional studies and from short-term followup. Also needed are long-term prospective studies that track episodes and the context in which they occur over time, assessment of the development of comorbid conditions, treatment-seeking behavior, medical care utilization and costs with and without treatment for panic disorder, as well as changes in functioning and the quality of life.

Methodological Studies

Currently, different measures, often idiosyncratic and some of undocumented quality, make comparison of subjects and results across studies difficult. More reliable, valid measures of all clinical features of panic disorder must be developed and standardized for general use. Similarly, there is a need for standardized methodologies for measuring all facets of outcome, including operational definitions of response, remission, recovery, and relapse.

Although field studies of diagnostic boundaries and criteria are ongoing, further research is required on the clinical definition of

panic disorder, including the validity of the diagnostic criteria and possible subtyping or variations of the disorder, which may have different natural histories or responses to treatment. Sensitive screening diagnostic instruments will be needed for population and genetic studies, prevention programs, and general clinical use.

Treatment Research

It is essential that recruitment strategies, success rates, and inclusion and exclusion criteria be very carefully and fully documented in each clinical research study.

Current information does not permit satisfactory comparison of the effectiveness and value of cognitive-behavioral and pharmacological treatments. Not only are multisite studies and comparable control groups needed, but cross-disciplinary studies within sites will facilitate interprofessional exchange of knowledge and skills. Multisite studies should be done in which psychosocial and pharmacological therapies are compared with each other and to combinations of the two. Further research is needed on optimal duration of treatment and on strategies to maintain treatment response. Studies are also needed to ascertain the type and extent of training of clinicians necessary for effective intervention. Studies are needed to assess patient match with treatment methods, including the sequencing of treatments.

Patients who drop out of clinical trials should be carefully followed. Some clinical drug trials also have revealed a high placebo response, suggesting that there are nonspecific psychosocial, unsystematic exposure instructions, or other unspecified factors that may have a potential influence on therapeutic outcomes.

Finally, new emphasis should be placed on prevention research programs for individuals at risk.

Basic Research

Current evidence supports familial prevalence, but there is only preliminary evidence for genetic transmission. Larger studies are needed to separate the genetic from the environmental contribution and to identify the most salient milieu influences (life events, family functioning, etc.). In such studies, there

should be a focus on identification of which diagnostic criteria are most likely to identify a genetic form of the disorder. Segregation studies should be done to determine likely patterns of transmission and to obtain estimates of genetic parameters necessary for the successful analysis of linkage studies.

Further basic studies of the biological and psychological underpinnings, as well as the influence of environmental factors associated with the disorder, are needed to understand its nature. Neurobiologic studies, including molecular approaches, and experimental studies of basic cognitive and behavioral processes will yield information and contribute to more effective treatment.

Conclusions and Recommendations

- Panic disorder is a distinct condition with a specific presentation, course, and positive family history and for which there are effective pharmacologic and cognitive-behavioral treatments.
- Treatment that fails to produce benefit within 6-8 weeks should be reassessed.
- Patients with panic disorder often have one or more comorbid conditions that require careful assessment and treatment.
- The most critical research needs are:
 - the development of reliable, valid, and standard measures of assessment and outcome;
 - the identification of optimal choices and structuring of treatments designed to meet the varying individual needs of patients; and
 - the implementation of basic research to define the nature of the disorder.
- Barriers to treatment include awareness, accessibility, and affordability.
- An aggressive educational campaign to increase awareness of these issues should be mounted for clinicians, patients and their families, the media, and the general public.

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"Discussion of Psychotherapy
Treatments"

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"Cognitive Therapy for Panic
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Allen Frances, M.D.

"Psychodynamic Treatment of
Panic Disorders"

Jack M. Gorman, M.D.

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George R. Heninger, M.D.

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Pharmacotherapy of Panic
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Wayne Katon, M.D.

"Primary Care Panic Disorder
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Heinz Katschnig, M.D.

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Thomas W. Uhde, M.D.

"Discussion of Pharmaco-
therapy"

Myrna M. Weissman, Ph.D.

"The Epidemiology and
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